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Incidence of urinary tract infections in infants with antenatally diagnosed hydronephrosis—A retrospective single center study

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ABSTRACT

Objective: To evaluate the incidence of urinary tract infections (UTIs) in infants with antenatal hydronephrosis (AHN).
Materials and Methods: A cohort of AHN patients admitted to our institution between 2003 and 2013 were identified. Altogether 192 patients with nonrefluxing hydronephrosis (HN, n = 135), nonrefluxing hydroureteronephrosis (HUN, n = 21), or vesicoureteral reflux (VUR, n = 36) were identified. Patients with complex anomalies or neonatal decompression of the urinary tract were excluded. Information about UTIs diagnosed among the AHN patients was collected and compared with data from 58 controls.
Results: During the median follow-up time of 2.6 (0.3–11.2) years, 24 (13%) patients (15 (10%) males and 9 (19%) females) and 2 (3%) controls experienced at least one UTI ($p = 0.033$). Eighteen (69%) UTIs were febrile. The males had the first UTI at significantly younger age than the females (0.3, 0.0–1.7 years vs. 1.0, 0.4–4.8 years, $p = 0.010$). UTI was detected in 15 (63%) patients with grade 4–5 VUR, in 8 (6%) patients with HN, and in one (5%) patient with HUN (p-values <0.001, 0.726 and >0.999 against the controls). None of the patients with grade ≤3 VUR had UTI. Fifty-eight percent of the patients with UTI were on antimicrobial prophylaxis. In five (12%) cases UTI appeared within one week after voiding cystourethrography (VCUG).
Conclusions: Infants with AHN and grade 4–5 VUR had the highest risk of UTI. UTIs tented to be more common in females than in males; however, males experienced UTI at younger age than females. VCUG caused UTI in 2.3% in our material.
Level of Evidence: III.

The prevalence of fetal hydronephrosis (HN) in antenatal ultrasonography (US) is approximately 1 % [1]. Antenatal hydronephrosis (AHN) may be caused by a variety of urological abnormalities from transient dilatation of the renal collection system to severe urinary tract obstruction and vesicoureteral reflux (VUR) [2,3]., Urinary tract abnormalities, particularly pyeloureteral obstruction (PUO), nonrefluxing hydroureteronephrosis (HUN), and vesicoureteral reflux (VUR), have been connected to increased risk of UTIs [4,5,6,7,8].

In this study, we evaluated retrospectively the frequency of UTI in a cohort of children with antenatally detected hydronephrosis. We aimed primarily to study (1) the risk of UTIs in children with different causes of AHN (VUR grades 1–3, VUR grades 4–5, nonrefluxing HUN, and HN alone) compared to children without any abnormality that is supposed to associate with UTIs, and (2) bacterial etiology and resistance in UTIs. Secondarily we analyzed the impact of surgical intervention on UTI risk in AHN patients.

1. Materials and methods

All patients with urinary tract abnormalities (ICD-10: Q60.0–Q64.9 and N13.0–N13.9) diagnosed between January 2003 and December 2013 were identified from the database of the Helsinki University Hospital using electronic search tools. We further selected manually all patients who had antenatally detected hydronephrosis to exclude patients who were diagnosed after UTI or other symptoms appearing postnatally. The ethics committee of the Helsinki University Hospital approved the study protocol.

A total of 192 patients with persistent HN (the postnatal anteroposterior diameter (APD) of renal pelvis >7 mm), nonrefluxing HUN (distal ureter visible on ultrasound examination), or VUR system were identified and included in the study (Table 1). None of the patients were circumcised. Renal US examination was performed on all patients, renal scintigraphy on 161 patients and voiding cystourethrography (VUCG) on 150 (78%) patients. VCUG was performed to a selected patient group according to our standard protocol: patients with (1) visible ureter in US or (2) pelvis APD ≥10 mm, (3) HN in association with reduced size kidney, or (4) bilateral hydronephrosis.

VUR was classified according to international classification [9]. In the case of bilateral VUR, the patient was classified according to the higher

Abbreviations: AHN, antenatal hydronephrosis; HN, hydronephrosis; HUN, hydroureteronephrosis; PUO, pyeloureteral obstruction; US, ultrasonography; UTI, urinary tract infection; VUR, vesicoureteral reflux; VCUG, voiding cystourethrography.

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Table 1
Total number of patients and gender distribution in AHN patients and controls.

Diagnostic group	Boys	Girls	Total
VUR gr 1–3, n (%)	8 (67)	4 (33)	12
VUR gr 4–5, n (%)	20 (83)	4 (17)	24
Nonrefluxing HUN, n (%)	16 (76)	5 (24)	21
HN, n (%)	100 (74)	35 (26)	135
All patients, n (%)	144 (75)	48 (25)	192
Controls, n (%)	38 (66)	20 (34)	58

VUR, vesicoureteral reflux; HUN, hydroureteronephrosis; HN, hydronephrosis.

grade. We excluded syndromatic patients and patients with complex urogenital abnormalities, ureteroceles, or urethral obstructions.

The control group consisted of 58 patients with suspected urinary tract abnormality and either normal postnatal renal US or abnormality supposedly not exposing to UTI (renal agenesis (n = 16), dysplastic or multicystic dysplastic kidney (n = 20), simple renal or ovarian cysts (n = 4), renal or adrenal cystic tumor (n = 2), ectopic kidney (n = 5) or adrenal hemorrhage (n = 1)). All patients with dysplastic kidneys were investigated with US, VCUG, and scintigraphy to exclude contralateral pathology.

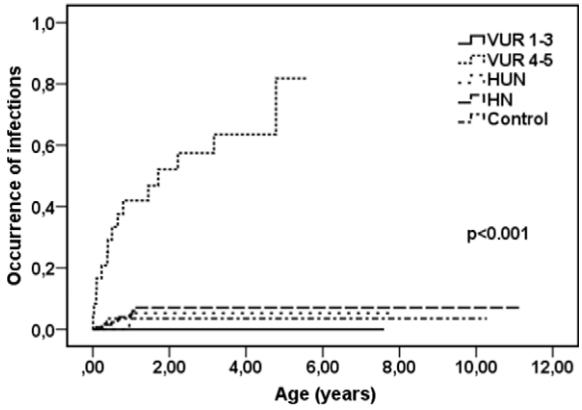
Information about age, gender, antimicrobial prophylaxis, results of imaging studies and possible urological surgery was collected. Antimicrobial prophylaxis was started according to our current protocol: (1) in patients with grade 3–5 VUR until they were toilet trained, (2) in patients with HN ≥10 mm of APD, or (3) in patients with dilated ureter without VUR until the first year of life. Occurrence of UTI was collected retrospectively from the patient journals and laboratory database. The diagnosis of UTI was defined as growth of a single pathogen on urine culture and significant pyuria (>60 × 10E9/L) in urinalysis. A bacterial count of 100,000 or more colony forming units (CFU)/mL in voided samples (clean catch urine, urine bag), ≥50,000 CFU/mL in a catheter sample, and any bacterial growth in suprapubic aspiration were considered significant. Bacterial growth in bag sample was confirmed by either suprapubic aspiration or catheter sample. In 13 patients the diagnosis was based on two consecutive bag urine samples and in two patients in one bag sample. Both of these two patients had clinical symptoms suggesting UTI, significant bacterial growth in urine and pyuria (>250–2063 × 10E9/L). Febrile UTI was defined as verified UTI together with fever (>38.5 °C), or CRP >35 mg/L [10]. The risk for UTI was calculated in each patient group during the follow-up time in our hospital. UTIs after surgery were analyzed separately in patients requiring surgical intervention.

The occurrence of UTIs is presented with Kaplan–Meyer curves. Patients' age and gender at the outset of the first UTI were compared between different diagnostic groups with Mann–Whitney test. Categorical variables were compared with Fisher's exact test. Statistical analyses were done with SPSS statistical package (IBM SPSS statistics 22).

2. Results

2.1. General findings

The median follow-up time for the AHN patients was 2.6 years (range 0.3–11.2 years) and that for the controls was 3.3 years (range 0.2–10.3 years) ($p = 0.533$). Two (3%) out of the 58 controls and 24 (13%) of the 192 patients had UTI before any operative intervention ($p = 0.051$). Females tented to have more UTIs than males (9/48 (19%) vs. 15/144 (10%), $p = 0.243$). The vast majority of the first-time UTIs (17/24 (71%)) were diagnosed during the first year of life (Fig. 1). The males had their first UTI at significantly younger age than the females (median 0.3 years; range 0.0–1.7 years vs. 1.0 years; range 0.4–4.8) years, $p = 0.010$). Nineteen (79%) of the 24 AHN patients and the other control patient with UTI had pyelonephritis.



Number of patients at risk

Age (years)	0.00	2.00	4.00	6.00	8.00	10.00
VUR 1-3	*12*	*9*	*5*	*1*	*0*	*0*
VUR 4-5	*24*	*9*	*4*	*0*	*0*	*0*
HUN	*21*	*13*	*8*	*5*	*0*	*0*
HN	*135*	*55*	*25*	*11*	*5*	*1*
Control	*58*	*41*	*20*	*12*	*4*	*1*

VUR, vesicoureteral reflux; HUN, hydroureteronephrosis; HN, hydronephrosis

Fig. 1. The occurrence of UTI in controls patients and AHN patients in different diagnostic groups.

2.2. UTIs in AHN subgroups

Patients with grade 4–5 VUR had significantly more UTIs than the patients with HUN, HN, or the control patients ($p < 0.001$, <0.001, <0.001 and <0.001 respectively). The UTI occurrence did not differ between the control patients and other patient groups except patients with gross VUR (Table 2). Female gender was a nonsignificant risk factor for UTI.

In our study 13 patients with HN had APD of renal pelvis between 7 and 10 mm. The UTI occurrence of patients with HN did not differ from controls when those particular patients were excluded ($p = 0.720$).

2.3. UTI bacteriology, recurrence and antimicrobial prophylaxis

Altogether 161 patients had initially continuous antibiotic prophylaxis. Twenty infections occurred during antibiotic prophylaxis. In 16 (80%) cases, the bacteria were resistant to the prophylactic antibiotic (Table 3). *Escherichia coli* caused 17 (71%) of the 24 first-time infections and only 4 (40%) of the 10 recurrent infections in the patients. In the controls, both infections were caused by *E. coli*, which was sensitive to all tested antibiotics.

Six of the 24 (25%) patients with UTI had recurrent infection without or before any operative intervention. Four (67%) of them had grade 4–5 VUR, one (17%) had HUN, and another had HN. Two patients with grade 4–5 VUR had two UTI recurrences and one child had three recurrent infections. There were no verified UTI recurrences in the control patients.

Altogether 215 VCUGs were done for the patients and controls. In five cases (2.3%), UTI was detected within one week after VCUG had been performed. From all three of these VCUG-related infections were first-time UTIs and two were recurrences. Four out of five patients had grade 4–5 VUR and one of them had HN. The patients with grade 4–5 reflux had pyelonephritis and the patient with HN had cystitis. All five patients were on antibiotic prophylaxis during VCUG before the UTI. According to our VCUG protocol patients receive therapeutic dose of antibiotics for three days. The prophylaxis starts in the morning of the examination day.

2.4. UTIs in AHN patients with surgical intervention

Forty-three (22%) patients underwent surgical intervention. Twelve (28%) of these patients had had at least one UTI before the first

Table 2
Occurrence of UTI in AHN patients and in controls.

	Females		Age at UTI		Males		Age at UTI		All patients		*p*-Value*
	n	UTI (%)	Median	Range	n	UTI (%)	Median	Range	n	UTI (%)	
VUR gr 1–3	4	(0)			8	(0)			12	(0)	>0.999
VUR gr 4–5	4	(100)	2.7	0.7–4.8	20	(55)	0.4	0.0–1.7	24	(63)	<0.001
HUN	5	(20)	1.0		16	(0)			21	(5)	>0.999
HN	35	[11]	0.84	0.5–1.1	100	[4]	0.5	0.1–1.0	135	[6]	0.726
Controls	20	[5]	0.4		38	[3]	0.2		58	[3]	

The data are presented in all patients and in females and males separately.
VUR, vesicoureteral reflux; HUN, hydroureteronephrosis; HN, hydronephrosis; UTI, urinary tract infection.
* Fisher's exact test, controls vs. all patients.

operation (9 patients with grade 4–5 VUR, one patient with HUN and two patients with HN). Despite successful surgery, UTI occurred at least once in 6 (14%) patients (in two cases after Deflux® treatment for grade 4–5 VUR, in one patient after ureteric tapering and neocystostomy because of obstructive HUN, and in 3 cases after pyeloplasty). Four of the operated patients had their first UTI after the surgical intervention. The median follow-up time after surgery was 2.9 (range 0.2–9.8) years and the median UTI occurrence time after surgery was 1.8 (range 0.1–7.5) years.

3. Discussion

In the present study, AHN was not found to be an independent risk factor for UTI, but the risk is depended on the underlying diagnosis. According to our findings infants with grade 4–5 VUR had significantly higher risk for UTIs than the control patients or any other patient group. On the contrary, the children with grade 1–3 VUR had no verified UTIs. The patients with nonrefluxing HN had a nonsignificant tendency to have more UTIs than the controls. There was also clear gender difference. Boys had UTIs at a significantly younger age than girls. However, girls tended to have more UTIs altogether during the follow-up period, but the difference was not significant. Our patients had also UTIs despite surgical treatment of grade 4–5 VUR or pyeloplasty for the patients with pyeloureteral obstruction. Sixty-three percent of the patients with grade 4–5 VUR and 6% of HN patients had UTI before any surgical treatment. After surgery 17% of the operated patients with grade 4–5 VUR and 11% with HN patients had UTI.

AHN may be associated with congenital renal dysplasia but AHN may also predispose to UTIs, which may in turn lead to further kidney damage [5,11]. In one large study with 822 patients with congenital urinary tract anomalies, 22% of the patients experienced UTI during the first year of life, the risk being increased particularly in girls [4]. In another study, hospitalization was needed during the first year of life because of pyelonephritis in 5% of infants with antenatal HN and in 1% of the patients without antenatal HN [7]. Our results are in line with these observations showing that 14% of the AHN patients and 3% of the controls had UTI during a median follow-up of about 3 years. It is for note, that 59% of the UTIs occurred in the patients with grade 4–5 VUR being the only patient group with increased risk for UTI.

In recent reports, the cutoff of 10 mm in APD has been suggested [12]. However, in children with significant nephrouropathies the postnatal APD may vary between 7 and 10 mm [13,14]. In the present study we primarily used 7 mm as cutoff level. The data were reanalyzed using 10 mm as cutoff level. However, no difference in the UTI prevalence could be found between these two cutoff levels.

The risk for UTIs seems to be very dependent on the underlying diagnosis in AHN patients. In our study, especially the patients with high-grade VUR had an increased risk for UTIs, similarly to earlier studies [8,15,16]. In the study by Evans et al. [8], 52% of the AHN patients with VUR had UTI despite continuous antibiotic prophylaxis. In their study, 52 of 54 patients had grade II–V reflux. Higher grades of VUR have also been linked to recurrent UTIs as well, similarly to our study [16]. In some studies, no connection is seen between antenatally detected VUR and UTIs. However, in these studies either the grade of VUR was not reported, or grade III VUR was interpreted as high-grade VUR [17,18].

HN together with urinary tract obstruction has been shown to increase the risk for UTIs [6,19]. It has also been shown that the severity of HN is positively correlated with the UTI risk [6,19]. In the present study we did not divide the patients based on the degree of HN. The patients with isolated HN, especially girls, had a tendency toward more UTIs than the control patients. However, this finding did not reach statistical significance. In our study, patients with HUN did not have an elevated risk for UTIs. However, in previous studies the results have been controversial. In one prospective study the patients with HUN and mild dilatation had a negligible risk for UTI whereas in another study there was a connection between nonrefluxing dilated ureters and UTIs [6,20].

In some earlier studies continuous antibiotic prophylaxis (CAP) reduced the risk of febrile UTIs in children with AHN because of ureteral dilatation, high-grade VUR, or ureterovesical junction obstruction [5,21,22,23]. A recent systematic review concluded that CAP is beneficial only in patients with high-grade hydronephrosis [24]. The risk for UTI was found to be 14.6% with antibiotic prophylaxis and 28.9% without prophylaxis. Another recent study with 405 patients with AHN showed that the risk for febrile UTI was 7.9% with antibiotic prophylaxis and 18.7% without antibiotic prophylaxis [5]. The risk factors for UTIs were high-grade VUR and ureterovesical obstruction. The major disadvantage of antimicrobial prophylaxis is an increased risk for antibiotic-resistant bacteria [22]. In our study, approximately half of the UTIs occurred during CAP; however, the design of our study did not allow us to estimate the effect of CAP because all of our patients were primarily put on CAP. However, if the previous observations concerning the benefits of

Table 3
Bacteria causing urinary tract infection and their resistance in all infections and depending on antimicrobial prophylaxis.

Bacteria	All infections	Trimethoprim		Nitrofurantoin		No prophylaxis	
	n	n	Resistant	n	Resistant	n	Resistant
*Escherichia coli**	24	11	11	0		13	3 for trimethoprim and 1 for cefalotin
Staphylococcus	5	4	3	0		1	1 for trimethoprim
Klebsiella†	3	2	1	0		1	
Enterococcus fecalis	2	2	1	0		0	
Coliform sp.	2	0	0	1	0	1	1 for cefalotin

* In one case there was additional growth of *Streptococcus agalactiae.*
† In one case there was additional growth of *E. fecalis.*

CAP are true, the real risk for UTIs in AHN patients is even greater than was observed in our study.

Our present study confirms the previous finding [8,15,16], that the patients with grade 4–5 VUR have an increased risk for UTIs. Despite this finding the justification for the evaluation of VUR remains controversial. VCUG probably caused UTI in 2.3% in our material and was a predisposing factor in 11% of all UTIs in the patient cohort. Accordingly, it might be preferable to perform VCUGs only in the patients with suspected high-grade VUR, and sufficient antibiotic prophylaxis should be given before and after the investigation. In the study, most of the patients were on trimethoprim prophylaxis at the time of VUCG. In some previous studies, the risk for UTI after VCUG has been 4–6% despite antibiotic prophylaxis [17,25].

Our study has some limitations. VCUG was performed in 77.1% of the patients and it is therefore possible that some patients with reflux were missed. On the other hand, only three of 43 patients without VCUG had an UTI. VCUG was performed according to our selection criteria in order to avoid unnecessary irradiation and distress for the patients and parents. In patients without VCUG, US findings were not suggestive for high grade VUR. Another caveat of the study are the nonuniform urine sample collection methods. In addition to suprapubic aspiration samples, we accepted also urine bag samples and samples taken by sterile catheterization. However, only urine bag samples with significant bacterial growth of a single uropathogen together with pyuria were considered as UTI. The major strength of this study is that we collected a well-defined cohort of AHN patients who were carefully followed up in a single center. None of the patients were lost from follow-up. Because of our centralized health care system it is likely that we have been able to collect all significant UTIs in this patient cohort. Additionally, we had bacteriological verification of all UTIs.

4. Conclusions

We conclude that infants with AHN together with grade 4–5 VUR are at the highest risk for UTI. The infections are more common in females but appear earlier in males. Seventy-one percent of first-time UTIs are caused by *E. coli*; however, 60% of the UTI recurrences were caused by non-*E. coli* pathogens, which should be taken into account in antimicrobial prophylaxis. The UTI recurrence rate was 25% before any operation and 17% after surgical intervention.

References

[1] Ek S, Lidefeldt KJ, Varricio L. Fetal hydronephrosis; prevalence, natural history and postnatal consequences in an unselected population. Acta Obstet Gynecol Scand 2007;86:1463.
[2] Nguyen HT, Herndon CDA, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. J Pediatr Urol 2010;6:212.
[3] Malik M, Watson AR. Antenatally detected urinary tract abnormalities: more detection but less action. Pediatr Nephrol 2008;23:897.
[4] Quirino IG, Diniz JS, Bouzada MC. Clinical course of 822 children with prenatally detected nephrouropathies. Clin J Am Soc Nephrol 2012;7:444.
[5] Herz D, Merguerian P, McQuiston L. Continuous antibiotic prophylaxis reduces the risk of febrile UTI in children with asymptomatic antenatal hydronephrosis with either ureteral dilation, high-grade vesicoureteral reflux, or ureterovesical junction obstruction. J Pediatr Urol 2014;10:650.
[6] Lee JH, Choi HS, Kim JK, et al. Non-refluxing neonatal hydronephrosis and the risk of urinary tract infection. J Urol 2008;179:1524.
[7] Walsh TJ, Hsieh S, Grady R, et al. Antenatal hydronephrosis and the risk of pyelonephritis hospitalization in the first year of life. Urology 2007;69:970.
[8] Evans K, Asimakadou M, Nwankwo O, et al. What is the risk of urinary tract infection in children with antenatally presenting dilating vesico-ureteric reflux? J Pediatr Urol 2015;11:93.e1.
[9] Lebowitz RL, Olbing H, Parkkulainen KV, et al. International system of radiographic grading of vesicoureteric reflux. International Reflux Study in Children. Pediatr Radiol 1985;15:105.
[10] Shaikh N, Craig JC, Rovers MM, et al. Identification of children and adolescents at risk for renal scarring after a first urinary tract infection: a meta-analysis with individual patient data. JAMA Pediatr 2014;168:893.
[11] Ylinen E, Ala-Houhala M, Wikström S. Risk of renal scarring in vesicoureteral reflux detected either antenatally or during the neonatal period. Urology 2003;61:1238.
[12] Bouzada MCF, Oliveira EA, Pereira AK, et al. Diagnostic accuracy of postnatal renal pelvic diameter as a predictor of uropathy: a prospective study. Pediatr Radiol 2004;34:798.
[13] Ismaili K, Avni FE, Wissing KM, et al. Long-term clinical outcome of infants with mild and moderate fetal pyelectasis: validation of neonatal ultrasound as a screening tool to detect significant nephrouropathies. J Pediatr 2004;144:759.
[14] Hálek J, Flögelová H, Michálková K, et al. Diagnostic accuracy of postnatal ultrasound screening for urinary tract abnormalities. Pediatr Nephrol 2010;25:281.
[15] Moriya K, Mitsui T, Kitta T, et al. Early discontinuation of antibiotic prophylaxis in patients with persistent primary vesicoureteral reflux initially detected during infancy: outcome analysis and risk factors for febrile urinary tract infection. J Urol 2015;193:637.
[16] Park S, Song SH, Lee C, et al. Bacterial pathogens in first febrile urinary tract infection affect breakthrough infections in infants with vesicoureteral reflux treated with prophylactic antibiotics. Urology 2013;81:1342.
[17] St Aubin M, Willihnganz-Lawson K, Varda BK, et al. Society for fetal urology recommendations for postnatal evaluation of prenatal hydronephrosis—will fewer voiding cystourethrograms lead to more urinary tract infections? J Urol 2013;190:1456.
[18] Moore SS, Bahat H, Rachmiel M, et al. Guidelines for urinary tract infections and antenatal hydronephrosis should be gender specific. Acta Paediatr 2015;104:e512.
[19] Coelho GM, Bouzada MC, Pereira AK, et al. Outcomes of isolated antenatal hydronephrosis: a prospective cohort study. Pediatr Nephrol 2007;22:1727.
[20] DiRenzo D, Persico A, DiNicola M, et al. Conservative management of prmary nonrefluxing megaureter during the first year of life: a longitudinal observational study. J Pediatr Urol 2015;11:226.e1.
[21] Estrada CR, Peters CA, Retik AB, et al. Vesicoureteral reflux and urinary tract infection in children with a history of prenatal hydronephrosis: should voiding cystourethrography be performed in cases of postnatally persistent grade II hydronephrosis? J Urol 2009;181:801.
[22] Wang HH, Gbadegesin RA, Foreman JW, et al. Efficacy of antibiotic prophylaxis in children with vesicoureteral reflux: systematic review and meta-analysis. J Urol 2015;193:963.
[23] Hoberman A, Chesney RW. RIVUR Trial Investigators. Antimicrobial prophylaxis for children with vesicoureteral reflux. N Engl J Med 2014;371:1072.
[24] Braga LH, Mijovic H, Farrokhyar F, et al. Antibiotic prophylaxis for urinary tract infections in antenatal hydronephrosis. Pediatrics 2013;131:e251.
[25] Rachmiel M, Aladjem M, Starinsky R, et al. Symptomatic urinary tract infections following voiding cystourethrography. Pediatr Nephrol 2005;20:1449.